Introduction

The tumor microenvironment (TME) contains high levels of tumor-secreted cytokines, which can drive the acquisition of T cell-inhibitory PD-L1 and PD-1 pathways. The PD-L1/PD-1 pathway is upregulated in male breast and lung cancer and is associated with poor prognosis (1). CD73, a PD-L1/PD-1 pathway target (2), can phosphorylate adenosine monophosphate (AMP) into adenosine (ADO). To probe cancer, PKP can also contribute to downstream activation.

Methods

Phase 1 Healthy Volunteer Study: This phase 1 healthy volunteer study consisted of single ascending dose (SAD) and repeated-dosing arms evaluating AB680 administered via a 30 to 60-minute intravenous (IV) infusion in the single-dosing arm, we evaluated single dose of 1, 5, 10, 15, 20, and 25 mg AB680. In the repeated-dosing arm, 3 doses of 8 mg AB680 were administered weekly (QW). The study involved 24 participants randomized 2:1:1:1:1:1.

Results

AB680 Pharmacokinetic Profile Supports 120W Dosing Frequency

CD73 Expression in Pancreatic Cancer Is One of the Highest Across Tumor Types

Conclusions

• AB680 has an excellent safety, PK/PK profile in healthy volunteers to support advancement into clinical trials with a QW dosing regimen.
• Pancreatic cancer tumors express high levels of CD73. KRAS, BRAF and KRAS-BRAF mutations correlate with elevated CD73 expression.
• Initiating Phase 1 safety-steady-state evaluation in combination with AB132 (clinical trial 121), germline and somatic PD-L1 positive 1% metastatic pancreatic cancer.
• A total of 20 patients in AB680 is in IND-enabling studies.

Formulation of AB680 Can Dramatically Increase Oral Exposure in Preclinical Species

AB680: Initial Study Targeting First-Line Pancreatic Cancer

Phase 1 Safety Study in Healthy Volunteers of AB680, a Small-Molecule Inhibitor of CD73 and Rationale for Combination Therapy in Patients with Gastrointestinal Malignancies

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